Supplementary Table S2. Animal studies of imaging in Rett syndrome with *MECP2* mutation

Imaging modality	Imaging phenotype	Animal model	Primary results	Reference
MRI	Volume measurement	Strain B6.129P2(C)-*MECP2*$^{tm1\text{-}1Bird}$ *MECP2 -/y* male mice	↓ A global reduction in brain size ↓ A reduction in cerebellum size ↓ Significantly thinner in some specific structures, especially the motor cortex and the corpus callosum	Saywell et al. 2006 (46)
	Volume measurement Segmentation of the mouse cerebellum in MRI cerebellar atlas	Homozygous females (*MECP2* 308 −/−), heterozygous females (*MECP2* 308 −/+), hemizygous males (*MECP2* 308 −/Y), and non-littermate WT from a C57BL/6 background.	The *MECP2* mutant mice had cerebellar volume changes that increased in scope depending on the genotype: hemizygous males to homozygous females	Steadman et al. 2014 (49)
	Voxelwise and regional-based analysis within segmented anatomical regions to determine the location, direction, and magnitude of the neuroanatomical differences	Male and female mice from the *MECP2*^{tm1Hzo}, *MECP2*$^{tm1.1Bird/J}$, and *MECP2*$^{tm2Bird/J}$ mouse lines	↓ Regardless of mutation type, regional volumes of the frontal, cingulate, sensory, motor cortices, the striatum, thalamus, and white matter tracts were smaller in mutant mice relative to their WT controls Regions of the cerebellum were differentially affected by the type of mutation: ↑ An increase in volume in the mutant *MECP2*^{tm1Hzo} brain relative to controls ↓ A decrease volume in the *MECP2*$^{tm1.1Bird/J}$ and *MECP2*$^{tm2Bird/J}$ lines	Allemang-Grand et al. 2017 (47)

DTI	FA, MD, AD, and RD were calculated Network topological organizations	Female RTT monkeys were generated using TALENs-based mutagenesis technique	↓ Decreased FA and increased RD values in WM tracts of bilateral posterior temporal, parietal, ventroposterior frontal, and right medial occipital lobes, as well as subcortical areas including striatum and thalamus ↓ Decreased FA and increased RD values of bilateral cingulum and corpus callosum Protracted early WM myelinization	Wang et al. 2021 (70)
PET	^{11}C-raclopride for D_2R imaging ^{11}C-MP for DAT analysis	*MECP2*-null mice, HET mice, WT mice	↓ Significantly reduced in HET mice and in *MECP2*-null mice compared to WT mice DAT varied by the type of analysis model used: ↓ The SRTM method showed a significant decrease in the BD_{ND} in *MECP2*-null mice compared to WT The LOGAN analysis model found significant age-related changes in BD_{ND} in WT mice that were not observed in *MECP2*-deficient mice	Wong et al. 2018 (82)
MRS	^{1}H MRS ^{31}P MRS	Strain B6.129P2(C)-*MECP2*$^{tm1\text{-}1Bird}$ *MECP2 -/y* male mice	↓ The low level of NAA, myo-inositol, and glutamine plus glutamate in *MECP2 -/y* mice ↑ Increased choline levels ↓ Reduction in ATP and PCr	Saywell et al. 2006 (46)

^{11}C-MP, ^{11}C-methylphenidate; AD, axial diffusivity; BP, binding potential; Cho, choline; Cr, creatine; D_2R, D_2 dopamine receptor; DAT, dopamine transporter; DTI, diffusion tensor imaging; FA, fractional anisotropy; *fin*, intraneurite volume fraction; GM, gray matter; HET, heterozygous; *irfrac*, isotropic

restricted volume fraction; *fiso*, isotropic fraction; MD, mean diffusivity; *MECP2*, methyl-CpG binding protein gene 2; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; NAA, N-acetyl aspartate; ODI, orientation–dispersion index; PCr, phosphocreatine; PET, positron emission tomography; RD, radial diffusivity; RTT, Rett syndrome; WM, white matter; WT, wild type.